ABSTRACT AMINO ISOXAZOLINE DERIVATIVES AND THEIR USE AS ANTI-DEPRESSANTS

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The invention concerns substituted amino isoxazoline derivatives, more in particular tricyclic dihydrobenzopyranoisoxazoline, dihydroquinolinoisozazoline, dihydronaphthalenoisoxazoline and dihydrobenzothiopyranoisoxazoline derivatives substituted on the phenylpart of the tricyclic moiety with primary, secondary and/or tertiary amino groups, according to Formula (I)

wherein $X = CH_2$, $N-R^7$, S or O, R^1 , R^2 and R^3 are certain specific substituents, with the proviso that at least one of R¹ and R² is an amino radical of formula N-R¹⁰R¹¹ wherein R¹⁰ and R¹¹ are each a variety of radicals. Pir is an optionally substituted piperidyl or piperazyl radical and R³ represents an optionally substituted aromatic homocyclic or heterocyclic ring system including a partially or completely hydrogenated hydrocarbon chain of maximum 6 atoms long with which the ring system is attached to the Pir radical and which may contain one or more heteroatoms selected from the group of O, N and S; a process for their preparation, pharmaceutical compositions comprising them and their use as a medicine, in particular for the treatment of depression and/of anxiety and disorders of body weight. The compounds according to the invention have surprisingly been shown to have a serotonin (5-HT) reuptake inhibitor activity in combination with additional α_2 -adrenoceptor antagonist activity and show a strong anti-depressant activity without being sedative. Compounds according to the invention are also suitable for treating depression, anxiety and body weight disorders. The invention also relates to novel combination of substituted amino isoxazoline derivatives according to the invention with antidepressants, anxiolytics and/or antipsychotics to improve efficacy and/or onset of action.

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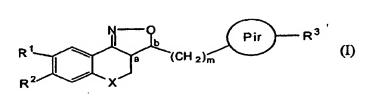
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(54) Title: SUBSTITUTED AMINO ISOXAZOLINE DERIVATIVES AND THEIR USE AS ANTI-DEPRESSANTS.



(57) Abstract: The invention concerns substituted amino isoxazoline derivatives according to Formula (I) wherein $X = CH_2$, N-R⁷, S or O, R¹, R² and R³ are certain specific substituents, with the proviso that at least one of R¹ and R² is an amino radical of formula N-R¹⁰ R¹¹ wherein R¹⁰ and R¹¹ are each a variety of radicals, Pir is an optionally substituted. piperidyl or piperazyl radical and

 R^3 represents an optionally substituted aromatic homocyclic or heterocyclic ring system; pharmaceutical compositions comprising them and their use as a medicine, in particular for the treatment of depression and/of anxiety and disorders of body weight. The compounds according to the invention have surprisingly been shown to have a serotonin (5-HT) reuptake inhibitor activity in combination with additional \propto_2 -adrenoceptor antagonist activity